

§ 1.136(a), and any fees required therefor (including fees for net addition of claims) are hereby authorized to be charged to our Deposit Account No. 19-0036.

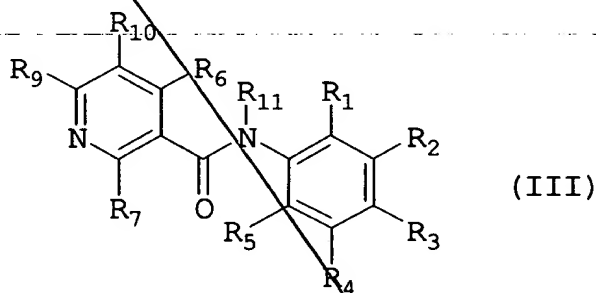
Amendments

In the Claims:

→ Please cancel claims 45, 49, 50, 53-57, 72-75, and 77 without prejudice or disclaimer to the subject matter thereof.

Please substitute the following claims 33, 42, 43, 46, 47, 58, and 76 for pending claims 33, 42, 43, 46, 47, 58, and 76:

33. (Twice Amended) A method of treating a disorder responsive to the induction of apoptosis in an animal suffering therefrom, comprising administering to a mammal in need of such treatment an effective amount of a compound of Formula III:



or a pharmaceutically acceptable salt or prodrug thereof, wherein

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R_1 - R_7 and R_9 - R_{10} are independently hydrogen, halo, haloalkyl, haloalkoxy, aryl, fused aryl, carbocyclic, fused carbocyclic, a heterocyclic group, fused heterocyclic, a heteroaryl group, alkyl, alkenyl, alkynyl, arylalkyl, arylalkenyl, arylalkynyl, heteroarylalkyl, heteroarylalkenyl, heteroarylalkynyl, carbocycloalkyl, heterocycloalkyl, hydroxyalkyl, nitro, aminoalkyl, cyano, cyanoalkyl, acyl, acylamido, hydroxy, thiol, acyloxy, azido, alkoxy, alkoxycarbonyl, aryloxy, arylalkoxy, carboxy, carbonylamido, alkylthiol, $-NH_2$, $-NHR_{15}$ or $-NR_{15}R_{16}$, wherein

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R_{15} and R_{16} are independently optionally substituted C_{1-10} alkyl, heterocyclic or heteroaryl groups; and

R_{11} is hydrogen; or alkyl, cycloalkyl, aryl or heteroaryl, each of which is optionally substituted;

wherein said disorder responsive to the induction of apoptosis is inflammation, inflammatory bowel disease, psoriasis, an autoimmune disease selected from the group consisting of rheumatoid arthritis, multiple sclerosis, diabetes mellitus, Hashimoto's thyroiditis, and autoimmune lymphoproliferative syndrome, or a cancer selected from the group consisting of Hodgkin's disease, non-Hodgkin's lymphoma, acute lymphocytic leukemia, chronic lymphocytic leukemia, multiple myeloma, neuroblastoma, breast carcinoma, ovarian carcinoma, lung carcinoma, Wilms' tumor, cervical carcinoma, testicular carcinoma, soft-tissue sarcoma, primary macroglobulinemia, bladder carcinoma, chronic granulocytic leukemia, primary brain carcinoma, malignant melanoma, small-cell lung carcinoma, stomach carcinoma, colon carcinoma, malignant pancreatic insulinoma, malignant carcinoid carcinoma, choriocarcinoma, mycosis fungoides, head or neck

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carcinoma, osteogenic sarcoma, pancreatic carcinoma, acute granulocytic leukemia, hairy cell leukemia, rhabdomyosarcoma, Kaposi's sarcoma, genitourinary carcinoma, thyroid carcinoma, esophageal carcinoma, malignant hypercalcemia, cervical hyperplasia, renal cell carcinoma, endometrial carcinoma, polycythemia vera, essential thrombocytosis, adrenal cortex carcinoma, skin cancer and prostatic carcinoma; and

wherein said prodrug is:

- B1
- a) an ester of a carboxylic acid containing compound of Formula III obtained by condensation with a C₁₋₄ alcohol;
 - b) an ester of a hydroxyl group containing compound of Formula III obtained by condensation with a C₁₋₄ carboxylic acid, C₃₋₆ dioic acid or anhydride thereof;
 - c) an imine of an amine group containing compound of Formula III obtained by condensation with a C₁₋₄ aldehyde or ketone; or
 - d) an acetal or ketal of at least one of the R₁₋₁₀ hydroxy containing groups obtained by condensation with chloromethyl methyl ether or chloromethyl ethyl ether;

provided that:

when R₁₋₂ and R₄₋₁₁ are hydrogen, R₃ is not optionally substituted pyrazolyl;

when R₁₋₅ are hydrogen, each of R₉ and R₁₀ is not phenyl;

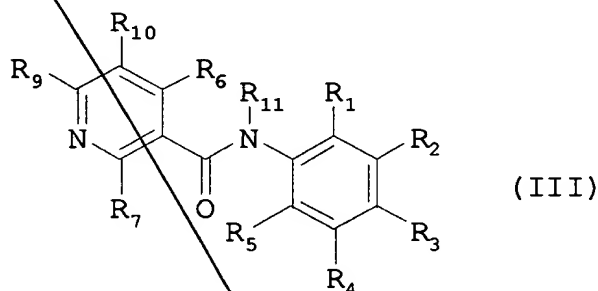
when R₃ is methoxy and R₅₋₁₁ are hydrogen, each of R₂ and R₄ is not cyclopentyloxy;

when R₁₋₃ and R₅₋₁₁ are hydrogen, R₄ is not optionally substituted alkyl;

when R₃₋₁₁ are hydrogen, R₁ and R₂ are not taken together to form optionally substituted thienyl-1,1-dioxide or partially saturated thienyl-1,1-dioxide; and

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when R₁ and R₄₋₁₁ are hydrogen, R₂ and R₃ are not taken together to form substituted
pyranyl.

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42. (Twice Amended) A method for treating cancer, comprising administering
to an animal in need of such treatment an effective amount of a compound of Formula III:



or a pharmaceutically acceptable salt or prodrug thereof, wherein

R₁-R₇ and R₉-R₁₀ are independently hydrogen, halo, haloalkyl, haloalkoxy, aryl, fused aryl, carbocyclic, fused carbocyclic, a heterocyclic group, fused heterocyclic, a heteroaryl group, alkyl, alkenyl, alkynyl, arylalkyl, arylalkenyl, arylalkynyl, heteroarylalkyl, heteroarylalkenyl, heteroarylalkynyl, carbocycloalkyl, heterocycloalkyl, hydroxyalkyl, nitro, aminoalkyl, cyano, cyanoalkyl, acyl, acylamido, hydroxy, thiol, acyloxy, azido, alkoxy, alkoxycarbonyl, aryloxy, arylalkoxy, carboxy, carbonylamido or alkylthiol, -NH₂, -NHR₁₅ or -NR₁₅R₁₆, wherein

R₁₅ and R₁₆ are independently optionally substituted C₁₋₁₀ alkyl, heterocyclic or heteroaryl groups; and;

R₁₁ is hydrogen; or alkyl, cycloalkyl, aryl or heteroaryl, each of which is optionally substituted;

wherein said cancer is selected from the group consisting of Hodgkin's disease, non-Hodgkin's lymphoma, acute lymphocytic leukemia, chronic lymphocytic leukemia, multiple

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myeloma, neuroblastoma, breast carcinoma, ovarian carcinoma, lung carcinoma, Wilms' tumor, cervical carcinoma, testicular carcinoma, soft-tissue sarcoma, primary macroglobulinemia, bladder carcinoma, chronic granulocytic leukemia, primary brain carcinoma, malignant melanoma, small-cell lung carcinoma, stomach carcinoma, colon carcinoma, malignant pancreatic insulinoma, malignant carcinoid carcinoma, choriocarcinoma, mycosis fungoides, head or neck carcinoma, osteogenic sarcoma, pancreatic carcinoma, acute granulocytic leukemia, hairy cell leukemia, rhabdomyosarcoma, Kaposi's sarcoma, genitourinary carcinoma, thyroid carcinoma, esophageal carcinoma, malignant hypercalcemia, cervical hyperplasia, renal cell carcinoma, endometrial carcinoma, polycythemia vera, essential thrombocytosis, adrenal cortex carcinoma, skin cancer and prostatic carcinoma; and

wherein said prodrug is:

- a) an ester of a carboxylic acid containing compound of Formula III obtained by condensation with a C₁₋₄ alcohol;
- b) an ester of a hydroxyl group containing compound of Formula III obtained by condensation with a C₁₋₄ carboxylic acid, C₃₋₆ dioic acid or anhydride thereof;
- c) an imine of an amine group containing compound of Formula III obtained by condensation with a C₁₋₄ aldehyde or ketone; or
- d) an acetal or ketal of at least one of the R₁₋₁₀ hydroxy containing groups obtained by condensation with chloromethyl methyl ether or chloromethyl ethyl ether;

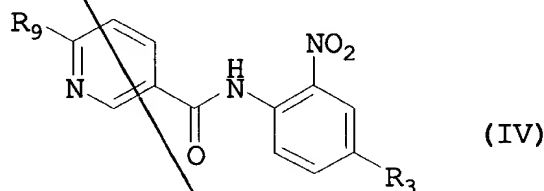
provided that:

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when R₁₋₂ and R₄₋₁₁ are hydrogen, R₃ is not optionally substituted pyrazolyl;
when R₁₋₅ are hydrogen, each of R₉ and R₁₀ is not phenyl;
when R₃ is methoxy and R₅₋₁₁ are hydrogen, each of R₂ and R₄ is not cyclopentyloxy;
when R₁₋₃ and R₅₋₁₁ are hydrogen, R₄ is not alkyl;
when R₃₋₁₁ are hydrogen, R₁ and R₂ are not taken together to form optionally substituted thienyl-1,1-dioxide or partially saturated thienyl-1,1-dioxide; and
when R₁ and R₄₋₁₁ are hydrogen, R₂ and R₃ are not taken together to form substituted pyranyl.

43. (Twice Amended) The method of claim 42, wherein said compound is of Formula IV:

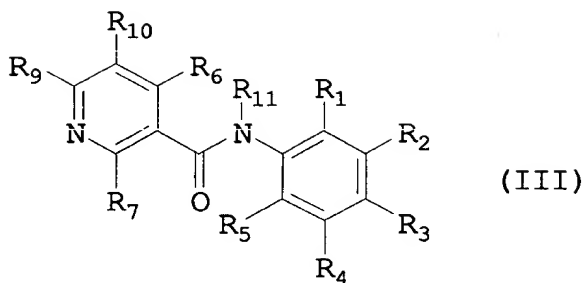


or a pharmaceutically acceptable salt or prodrug thereof.

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46. (Twice Amended) A method for the treatment of drug resistant cancer, comprising administering to an animal in need of such treatment an effective amount of a compound of the Formula III:

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or a pharmaceutically acceptable salt or prodrug thereof, wherein:

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R_1 - R_7 and R_9 - R_{10} are independently hydrogen, halo, haloalkyl, haloalkoxy, aryl, fused aryl, carbocyclic, fused carbocyclic, a heterocyclic group, fused heterocyclic, a heteroaryl group, alkyl, alkenyl, alkynyl, arylalkyl, arylalkenyl, arylalkynyl, heteroarylalkyl, heteroarylalkenyl, heteroarylalkynyl, carbocycloalkyl, heterocycloalkyl, hydroxyalkyl, nitro, aminoalkyl, cyano, cyanoalkyl, acyl, acylamido, hydroxy, thiol, acyloxy, azido, alkoxy, alkoxycarbonyl, aryloxy, arylalkoxy, carboxy, carbonylamido or alkylthiol, $-NH_2$, $-NHR_{15}$ or $-NR_{15}R_{16}$, wherein

R_{15} and R_{16} are independently optionally substituted C_{1-10} alkyl, heterocyclic or heteroaryl groups; and; and

R_{11} is hydrogen; or alkyl, cycloalkyl, aryl or heteroaryl, each of which is optionally substituted;

wherein said drug resistant cancer is selected from the group consisting of Hodgkin's disease, non-Hodgkin's lymphoma, acute lymphocytic leukemia, chronic lymphocytic leukemia, multiple myeloma, neuroblastoma, breast carcinoma, ovarian carcinoma, lung carcinoma, Wilms' tumor, cervical carcinoma, testicular carcinoma, soft-tissue sarcoma, primary macroglobulinemia, bladder carcinoma, chronic granulocytic leukemia, primary brain carcinoma, malignant melanoma, small-cell lung carcinoma, stomach carcinoma, colon

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carcinoma, malignant pancreatic insulinoma, malignant carcinoid carcinoma, choriocarcinoma, mycosis fungoides, head or neck carcinoma, osteogenic sarcoma, pancreatic carcinoma, acute granulocytic leukemia, hairy cell leukemia, rhabdomyosarcoma, Kaposi's sarcoma, genitourinary carcinoma, thyroid carcinoma, esophageal carcinoma, malignant hypercalcemia, cervical hyperplasia, renal cell carcinoma, endometrial carcinoma, polycythemia vera, essential thrombocytosis, adrenal cortex carcinoma, skin cancer and prostatic carcinoma; and

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wherein said prodrug is:

- a) an ester of a carboxylic acid containing compound of Formula III obtained by condensation with a C₁₋₄ alcohol;
- b) an ester of a hydroxyl group containing compound of Formula III obtained by condensation with a C₁₋₄ carboxylic acid, C₃₋₆ dioic acid or anhydride thereof;
- c) an imine of an amine group containing compound of Formula III obtained by condensation with a C₁₋₄ aldehyde or ketone; or
- d) an acetal or ketal of at least one of the R₁₋₁₀ hydroxy containing groups obtained by condensation with chloromethyl methyl ether or chloromethyl ethyl ether;

provided that:

when R₁₋₂ and R₄₋₁₁ are hydrogen, R₃ is not optionally substituted pyrazolyl;

when R₁₋₅ are hydrogen, each of R₉ and R₁₀ is not phenyl;

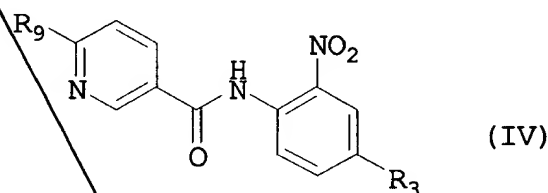
when R₃ is methoxy and R₅₋₁₁ are hydrogen, each of R₂ and R₄ is not cyclopentyloxy;

when R₁₋₃ and R₅₋₁₁ are hydrogen, R₄ is not alkyl;

when R₃₋₁₁ are hydrogen, R₁ and R₂ are not taken together to form optionally substituted thienyl-1,1-dioxide or partially saturated thienyl-1,1-dioxide; and

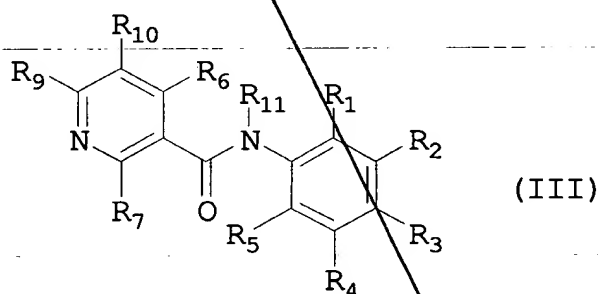
when R₁ and R₄₋₁₁ are hydrogen, R₂ and R₃ are not taken together to form substituted pyranyl.

47. (Twice Amended) The method of claim 46, wherein said compound is of Formula IV:



or a pharmaceutically acceptable salt or prodrug thereof.

58. (Twice Amended) A compound of Formula III:



or a pharmaceutically acceptable salt or prodrug thereof, wherein

R₁ and R₅ are independently selected from the group consisting of hydrogen, hydroxy, alkyl, alkoxy, halogen, NO₂, cyano, haloalkyl, haloalkoxy, amino and aminoalkyl,

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provided that at least one of R₁ and R₅ is selected from the group consisting of NO₂, cyano, alkyl and haloalkyl;

R₂ and R₄ are independently selected from the group consisting of hydrogen, hydroxy, halogen, cyano, haloalkyl, haloalkoxy, amino and aminoalkyl;

R₃ is alkyl, Cl, F, haloalkyl, alkoxy, arylalkoxy, cyano, haloalkyloxy, amino or aminoalkyl;

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R₆ is hydrogen, hydroxy, alkyl, NO₂, cyano, haloalkyl, haloalkyloxy, amino or aminoalkyl;

R₇ is hydrogen, hydroxy, alkyl, NO₂, cyano, haloalkyl, haloalkyloxy, amino or aminoalkyl;

R₉ is hydroxy, alkyl, halogen, NO₂, haloalkyl, alkoxy, cyano, haloalkyloxy, amino or aminoalkyl;

R₁₀ is hydrogen, hydroxy, alkyl, Cl, F, NO₂, cyano, haloalkyl, haloalkyloxy, amino or aminoalkyl; and

R₁₁ is hydrogen, alkyl or haloalkyl;

wherein said prodrug is:

- a) an ester of a carboxylic acid containing compound of Formula III obtained by condensation with a C₁₋₄ alcohol;
- b) an ester of a hydroxyl group containing compound of Formula III obtained by condensation with a C₁₋₄ carboxylic acid, C₃₋₆ dioic acid or anhydride thereof;
- c) an imine of an amine group containing compound of Formula III obtained by condensation with a C₁₋₄ aldehyde or ketone; or

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d) an acetal or ketal of at least one of the R_{1-10} hydroxy containing groups obtained by condensation with chloromethyl methyl ether or chloromethyl ethyl ether;

provided that when R_2 and R_4 are hydrogen and each of R_9 and R_{10} is halo, R_1 and R_3 are not both alkyl.

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76. (Once Amended) The method of any one of claims 33, 42, and 46 wherein optional substituents on the alkyl or heteroaryl group of R_{15} and R_{16} or the alkyl, aryl, or heteroaryl group of R_{11} include one or more halo, C_1 - C_6 haloalkyl, C_6 - C_{10} aryl, C_4 - C_7 cycloalkyl, C_1 - C_6 alkyl, C_2 - C_6 alkenyl, C_2 - C_6 alkynyl, C_6 - C_{10} aryl(C_1 - C_6)alkyl, C_6 - C_{10} aryl(C_2 - C_6)alkenyl, C_6 - C_{10} aryl(C_2 - C_6)alkynyl, C_1 - C_6 hydroxyalkyl, nitro, amino, ureido, cyano, C_1 - C_6 acylamino, hydroxy, thiol, C_1 - C_6 acyloxy, azido, C_1 - C_6 alkoxy or carboxy.
